Remarks

I. Status of the claims

Claims 1, 4, 7-9, 11, 12, 23, 28-31, and 33 are pending and stand rejected. Claims 1, 8, 9, 23, 30 and 33 have been amended, and new claims 34 to 36 have been added.

Applicants thank the Examiner for the helpful telephone interview on March 5, 2009, with the Examiner and the Supervisory Patent Examiner, in which the claims and cited references were discussed. Also discussed was the possibility of obtaining comparative data and further claim amendments.

II. Amendments to the claims

Claim 1 has been amended for clarity by deleting the term "about 0<10%" and replacing it with between 0 and 10 %. Similar limitations have been amended in the same manner in claims 8, 9, and 30. Claim 1 has also been amended for clarity by deleting the term "matrix" and replacing it with the term "homogenous mixture." Support for this amendment can be found at page 5, lines 1-12, which explains that the components of the tablet are intimately blending to forma homogenous mixture. Claims 9, 23, 30 and 33 have similarly been amended.

New claims 34 to 36 depend from claim 1, and recite certain percentages of hydroxyethylcellulose and hydroxypropyl methylcellulose. Support for these amendments can be found in the examples. Specifically, example 1 provides 25 % of hydroxyethyl cellulose, while examples 2 and 3 provide 35 % hydroxypropyl methylcellulose. Applicants further note that "[w]ith respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure." M.P.E.P. § 2163.05. Applicants submit that the range about 1 to 25 % by weight of

hydroxyethyl cellulose and 1 to 35 % by weight of hydroxypropyl methyl cellulose is inherently supported by the specification. In *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25%- 60%" and specific examples of "36%" and "50%." A new claim limitation of "between 35% and 60%" met the description requirement. For the same reasons, new claims 34 to 36 is supported by the examples.

No new matter has been added by these amendments.

III. Claim Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner states that the claim term "about 1 to 58 % by weight of a mixture of hydroxyethyl cellulose and hydroxypropyl methyl cellulose represents new matter. Applicants respectfully traverse. As noted in the response filed on September 12, 2008, "[w]ith respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure." M.P.E.P. § 2163.05. Applicants submit that the range about 1 to 58% by weight of a mixture of hydroxyethyl cellulose and hydroxypropyl methyl cellulose is inherently supported by the specification. In *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25%-60%" and specific examples of "36%" and "50%." A new claim limitation of "between 35% and 60%" met the description requirement. Similarly, the limitation of about 1 to 58% by weight is supported by the examples. Specifically, example 1 describes a formulation with 58% HEC/HMPC, Example 2 discloses 50% HEC/HMPC and example 3 discloses 55% HEC/HMPC. Thus, the specification as filed provides ample support for the recited range.

The Examiner also states that claims 1, 4, 7-9 and 12 are indefinite because of the recitation of "delivery of a selected pharmaceutically active substance." According to the Examiner "it is not clear what is being selected." *Office Action* at p. 5. Although Applicants disagree, the term "selected" has been deleted from the present claims.

The Examiner also states that the term "about 0<10% by weight of talc" is unclear. Applicants note that symbol "<" is a commonly used mathematical symbol, and as used in claims, denotes that the amount is greater than 0, but less than 10 %. Nevertheless, claim 1 has been amended to recite "between 0 and 10 % by weight of talc." This change has been similarly applied to the amount of magnesium stearate, and has been made throughout all of the claims where the symbol "<" was used. Applicants further submit that "0<10%" has the same meaning as "between 0 and 10%." Accordingly, no new matter has been added.

For the reasons set forth above, Applicants respectfully request withdrawal of the rejections under § 112.

IV. Rejections under 35 U.S.C. § 103

The Examiner has rejected the claims as being obvious over U.S. Patent No. 4,252,786 to Weiss et al. ("Weiss") in view of U.S. Patent No. 4,940,587 to Jenkins et al. ("Jenkins"). The Examiner states that "with regards to claims 1, 9, 23, 30 and 33 (in parts), 4 and 8 a rate release medicament from a controlled release tablet comprising polymers of acrylic acid cross linked with polyalkenyl alcohols." *Office Action* at p. 7. The Examiner relies on Jenkins for allegedly "show[ing] that the mixture of hydroxyethylcellulose and hydroxypropylcellulose is well known in the pharmaceutical controlled release art." *Office Action* at p. 8. The Examiner further states that the skilled artisan "would have been motivated to combine the Weiss and Jenkins to formulation a

controlled release drug that comprises an acrylic acid cross linked with polyalkenyl alcohol, comprising 2-15 % of hydroxypropylmethylcellulose and hydroxyethyl cellulose in a matrix with magnesium state and talc because these agents are well known in the art of formulating a controlled release drug." *Office Action* at p. 8-9. Applicants respectfully traverse.

In order to establish a *prima facie* case of obviousness, the Examiner must determine the scope and content of the prior art, ascertain the differences between the claimed invention and the prior art and resolve the level of ordinary skill in the pertinent art. *Graham v. John Deere Co.*, 383 U.S. 1, 148 (1966). Once the Graham factual inquiries have been resolved, the Examiner must explain why the differences between the cited references and the claims would have been obvious to one of ordinary skill in the art. Fed. Reg. Vol. 72, No. 195, p. 57527. The Supreme Court in *KSR* stressed that "obviousness cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR* 127 S.Ct. 1727, 1740 (2007); see also Fed. Reg. Vol. 72, No. 195, p. 57529. "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious." Fed. Reg. Vol. 72, No. 195 at p. 57528. Additionally, objective evidence of nonobviousness must be considered. Such evidence, sometimes referred to as ''secondary considerations,'' may include evidence of commercial success, long-felt but unsolved needs, failure of others, and unexpected results. *Id.*

Weiss describes a tablet having a polymeric vinylpyrrolidinone carboxyvinyl hydrophilic core coated with a relatively insoluble, water permeable film, wherein the film comprises a combination of hydrophobic and hydrophilic polymers. *Weiss* at col. 1, ll. 38-48. The hydrophilic

polymers can be cellulose methyl ethers, including hydroxypropylmethyl cellulose. *Id.* at col. 3, ll. 65-67.

Weiss fails to disclose 1-58% by weight of a mixture of hydroxyethyl cellulose and hydroxypropyl methylcellulose provided as a homogenous mixture with the other tablet ingredients, as recited in the amended claims. Specifically, the hydroxypropyl methylcellulose described in Weiss is provided as a part of a coating solution, which is applied to the tablet, and is not a part of the matrix. Carbopol 934, meanwhile, is a part of the Weiss tablet core. Thus, these two ingredients cannot be considered to be "provided as a homogenous mixture," as recited in the instant claims.

Jenkins fails to remedy the deficiencies of Weiss. Contrary to the Examiner's statement, Jenkins does not provide a mixture of hydroxyethyl cellulose and hydroxypropyl methylcellulose. Rather, Jenkins describes "granules of a higher aliphatic alcohol and a hydrated water-soluble hydroxyalkyl cellulose having a drug distributed therethrough and being coated with a cellulose derivative which is adherent to the mucosa." *Jenkins* at col. 1, ll. 51-56 (emphasis added). Thus, Jenkins fails to disclose a mixture of hydroxyethyl cellulose and hydroxypropyl methylcellulose. Furthermore, like Weiss, Jenkins also separates the ingredients between the core and the coating, rather than providing them together as a homogenous mixture.

As described in the Declaration under C.F.R. § 1.132 by Odidi et al. ("the Declaration"), the present claims provide all of the recited components as a homogenous mixture, which is then formulated into a tablet. The resulting tablet has distinct release profile that is not achieved by, nor suggested by, the teachings of Weiss and Jenkins, which separate certain components into a coating. Specifically, the Declaration describes a comparative experiment between a tablet prepared

according to Weiss and a tablet prepared according to the present invention, each containing Metformin as the pharmaceutical ingredient. *Declaration* at ¶¶ 6-7; Tables 1-3. The dissolution of each of the tablets was then studied over a 13 hour period of time, and demonstrate the different release profiles. The results demonstrate that the Weiss tablet releases the Metformin in two steps. First, there is a lag phase for almost an hour, followed by a relatively fast rate of release. *Declaration* at ¶ 10; Table 5; Figure 1. In contrast, the tablet from the present application provides a one step process, wherein the drug begins to be released almost immediately, and continues to be released at a relatively steady rate, over a longer period of time compared to the Weiss tablet. *Declaration* at ¶ 11; Table 5; Figure 1. As depicted in Figure 1 of the Declaration, nearly 100 % of the drug is released by the Weiss tablet at 4 hours, while a little over 80 % of the drug is released by the claimed formulation at 4 hours. Thus, the presently claimed formulation provides unexpected results over the cited references.

In light of the amendments and remarks set forth above, Applicants respectfully request withdrawal of this rejection.

V. Provisional Non-Statutory Double Patenting

Claims 1, 4, 7-12, 23 and 28-33 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent Application No. 11/473,386 ("the '386 application"). Claims 1, 4, 7-12, 23 and 28-33 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 7,090,867. Applicants respectfully request that the Examiner hold in abeyance this obviousness-type double patenting rejection until allowable subject matter is indicated, at which point Applicants will file a terminal disclaimer if necessary.

VI. Conclusion

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conference would be helpful, the Examiner is invited to call the undersigned at 617-832-1223. Applicants hereby request that any additional fees required for timely consideration of this application be charged to **Deposit Account No. 06-1448, Reference SMI-005.01.**

Dated: May 13, 2009

Respectfully submitted,

/Hilary Dorr Lang/
Hilary Dorr Lang
Registration No.: 51,917
FOLEY HOAG LLP
155 Seaport Blvd
Boston, Massachusetts 02210
(617) 832-1223
Attorney for Applicants